

09/694,701

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L1: Entry 10 of 148

File: USPT

Oct 30, 2001

DOCUMENT-IDENTIFIER: US 6309829 B1

TITLE: Length determination of nucleic acid repeat sequences by discontinuous primer extension

DEPR:

When primers are separately synthesized, and subsequently attached to a solid phase support for use, the primer may be attached to the support through a covalent linkage or a non-covalent linkage. When the primer is attached to the solid support through a non-covalent linkage, the primer includes one member of specific binding pair, e.g., biotin, the other member of the pair being attached to the solid support, e.g., avidin. Several methods are available for covalently linking polynucleotides to solid supports, e.g., through reaction of a 5'-amino polynucleotide with an isothiocyanate-functionalized glass support (Guo). A wide range of exemplary linking moieties for attaching primers onto solid supports either covalently or non-covalently are disclosed elsewhere. (Pon; Webb; Barany; Damha; Beattie; Maskos and Southern).

WEST[Generate Collection](#)**Search Results - Record(s) 11 through 12 of 12 returned.**☐ 11. Document ID: US 5254458 A

L3: Entry 11 of 12

File: USPT

Oct 19, 1993

US-PAT-NO: 5254458

DOCUMENT-IDENTIFIER: US 5254458 A

TITLE: Immunoassays using antigens produced in heterologous organisms

DATE-ISSUED: October 19, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mimms; Larry T.	Lake Villa	IL		

US-CL-CURRENT: 435/5; 435/7.1, 435/7.92, 435/7.94, 435/973, 435/974, 436/820

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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☐ 12. Document ID: US 5011861 A

L3: Entry 12 of 12

File: USPT

Apr 30, 1991

US-PAT-NO: 5011861

DOCUMENT-IDENTIFIER: US 5011861 A

TITLE: Membranes for solid phase protein sequencing

DATE-ISSUED: April 30, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Coull; James M.	Acton	MA		
Rappin; Darryl J.	North Billerica	MA		
Koester; Hubert	Concord	MA		
Pluskal; Malcolm G.	Bedford	MA		
Steuck; Michael J.	North Reading	MA		
Bonner; Alex G.	Lexington	MA		

US-CL-CURRENT: 521/53; 521/54

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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Term	Documents
MODIF\$3	0
MODIF.DWPI,EPAB,JPAB,USPT.	496
MODIFA.DWPI,EPAB,JPAB,USPT.	1
MODIFATN.DWPI,EPAB,JPAB,USPT.	1
MODIFCN.DWPI,EPAB,JPAB,USPT.	22
MODIFCNS.DWPI,EPAB,JPAB,USPT.	1
MODIFD.DWPI,EPAB,JPAB,USPT.	9
MODIFE.DWPI,EPAB,JPAB,USPT.	3
MODIFED.DWPI,EPAB,JPAB,USPT.	714
MODIFEDS.DWPI,EPAB,JPAB,USPT.	1
(L1 AND (MODIF\$3 NEAR5 (SOLID\$1 OR ARRAY\$1 OR BEAD\$1))).USPT,JPAB,EPAB,DWPI.	12

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12

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L3: Entry 10 of 12

File: USPT

Apr 23, 1996

DOCUMENT-IDENTIFIER: US 5510084 A

TITLE: Process for immobilizing a nucleic acid fragment by passive attachment to a solid substrate, the solid substrate thus obtained, and its use

BSPR:

The term "solid support" as used here includes all the materials on which a nucleic acid fragment may be immobilized for use in diagnostic tests, in affinity chromatography and in separation processes. Natural or synthetic materials, which may or may not be chemically modified, may be used as solid support, in particular polysaccharides such as cellulose materials, for example paper, cellulose derivatives, such as cellulose acetate and nitrocellulose; polymers, such as polyvinyl chloride, polyethylene, polystyrenes or polyacrylate, or copolymers, such as vinyl chloride/propylene polymer or vinyl chloride/vinyl acetate polymer; copolymers based on styrenes; natural fibers, such as cotton, and synthetic fibers, such as nylon. The support can be modified by irradiation.

CLPR:

1. A process for immobilization by non-covalent attachment to a solid support, of a nucleic acid fragment containing less than 100 nucleotides, comprising: forming a derivative from the covalent coupling of said fragment with a ligand having a molecular mass of less than 5000 and containing at least one amine group, and depositing said derivative on the support, said derivative not being capable of forming a covalent bond with said support under conditions of said depositing, with the proviso that when said ligand is a nucleotide or oligonucleotide it comprises at least one nucleotide modified so as to introduce said amine group.

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L3: Entry 8 of 12

File: USPT

Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830655 A

TITLE: Oligonucleotide sizing using cleavable primers

BSPR:

For modified primers including an immobilization attachment site, the primer is attachable to a solid support by either a covalent or non-covalent linkage between the solid support and the primer immobilization attachment site to provide an immobilized modified oligonucleotide composition. Solid supports for use in the present invention include glass, silicon, polystyrene, cellulose, teflon, polystyrene divinyl benzene, aluminum, steel, iron, copper, nickel, silver and gold.

DRPR:

FIGS. 5A-5E illustrate four alternate embodiments of an immobilized cleavable primer in accordance with the invention: FIG. 5A presents an immobilized modified primer having two regions connected by a cleavable site, X; FIG. 5B illustrates a biotin molecule connected to the 5' end of a modified primer; FIG. 5C illustrates capture of a modified primer prior to enzymatic extension on an avidin-functionalized solid support; FIG. 5D represents a modified primer affixed to a solid support through a 5-allylamino substituent at the 5 position of a uracil; FIG. 5E presents a modified primer containing a terminal ribose cleavage site, X;

DEPR:

An "immobilization attachment site" or IAS is a site which may be present within an oligonucleotide primer for binding to a solid support material either directly, through an intervening spacer arm, or by specific hybridization to an intermediary oligonucleotide which is bound to a solid support. The immobilization attachment site may be located either upstream (i.e., 5' to) or downstream (i.e., 3' to) of the cleavable site and may require chemical modification prior to binding to the solid support. Alternatively, the immobilization attachment site may be contained within the extension segment resulting from an enzymatic extension reaction, or, may be contained within a target nucleic acid. The immobilization attachment site can be a select functional group for covalent bonding to a solid support, such as those representative functional groups shown in FIGS. 2A-2K, and FIG. 2M. The immobilization attachment site can also be a ligand such as biotin, for attachment via a high-affinity non-covalent interaction with a solid support. Further, the immobilization attachment site can also be composed of a series of bases complementary to an intermediary oligonucleotide. Immobilization of the modified primer is effected, for example, by specific hybridization of the immobilization attachment site to an intermediary oligonucleotide, which is bound to a solid support. The intermediary oligonucleotide may also act as the template. The immobilization attachment site may be attached to the solid support by either chemical or enzymatic means. Upon attachment of the immobilization attachment site to a solid support, the resulting immobilization linkage is one which remains stable under the conditions employed for cleaving the cleavable site and does not inhibit base pair hybridization nor block the ability to extend the primer from its 3' end.

DEPR:

FIG. 5D illustrates an alternate embodiment of the invention in which the modified primer is attached to a solid support through an immobilization

attachment site present as a substituent on one of the heterocyclic bases. As shown in FIG. 5D, the site for immobilization is an amino residue substituted at the 5 position of a uracil (Dattagupta, 1989), and more specifically, is a 5-allylamino substituent. The amino group may be in protected form (e.g., trifluoroacetamido) prior to attachment to the solid support. As indicated, immobilization to the solid support is through an amide linkage, although any of a number of immobilization attachment linkages may be used, as will be described in more detail below. Coupling of the amino residue to a solid support is generally carried out by using an activated support material, such as an N-hydroxysuccinimide (NHS) ester functionalized support.

DEPR:

The immobilization attachment site can be a select functional group for covalent bonding to a solid support, such as those representative functional groups shown in FIGS. 2A-2K, and FIG. 2M. The immobilization attachment site can also be a ligand such as biotin, for attachment via a high-affinity non-covalent interaction with a solid support.

DEPR:

Solid support materials for use in coupling to an oligonucleotide include functionalized supports such as the 1,1'-carbonyldiimidazole activated supports available from Pierce (Rockford, Ill.) or functionalized supports such as those commercially available from Chiron Corp. (Emeryville, Calif.). Solid supports for use in the present invention include matrix materials such as 6% cross-linked agarose, Trisacryl GF-2000 (a hydrophilic matrix material) and TSK HW-65F, all activated with 1,1'-carbonyldiimidazole (Pierce). Immobilization is typically carried out by reacting a free amino group of an amino-modified oligonucleotide with the reactive imidazole carbamate of the solid support. Displacement of the imidazole group results in formation of a stable N-alkyl carbamate linkage between the oligonucleotide and the support as shown in FIG. 2B. Coupling is usually carried out at pHs ranging from 9-11 although a pH range from 9.5-10 is preferable. Coupling to pH sensitive materials may be carried out in buffer at pHs around 8.5.

DEPR:

Amino-modified oligonucleotides for use in attaching to a solid support may be synthesized using standard solid phase DNA synthesis methodologies employing, for example, the modified nucleoside phosphoramidite Amino-Modifier-dT (Glen Research, Sterling Va.), which contains a base labile trifluoroacetyl group protecting a primary amine attached to thymine via a 10-atom spacer arm, phosphoramidite 5'-Amino-Modifier C6 (Glen Research, Sterling Va.), which contains a primary amino group protected with an acid labile monomethoxytrityl group, or N-trifluoroacetyl-6-aminoethyl-2-cyanoethyl N',N'-isopropylphosphoramidite (Applied Biosystems, Foster City, Calif.). Although amino-containing oligonucleotides are most commonly prepared using phosphoramidite chemistry, any other method which leads to oligonucleotides containing primary amine groups may also be used.

DEPR:

In another immobilization approach, aldehyde groups of a modified oligonucleotide are coupled to hydrazide groups on a solid matrix as shown in FIG. 2J. A primary hydroxyl group on an oligonucleotide is first oxidized to the corresponding aldehyde, typically with a mild oxidant such as sodium periodate. The oligonucleotide is then coupled to a hydrazide-containing matrix such as Pierce's CarboLink.TM. Hydrazide. The coupling reaction is performed at neutral pH.

DEPR:

The method employed for determining the sequence of a target oligonucleotide strand will often involve Sanger-type sequencing using the modified cleavable primers of the present invention. Immobilization of the modified primer on the solid support may take place either before or after the enzymatic extension reactions.

DEPR:

A typical DNA sequencing reaction using the Sanger method proceeds as follows. The reaction consists of a target DNA strand to be sequenced, a modified primer containing a cleavable site in accordance with the invention, and that is complementary to the end of the target strand, a carefully controlled ratio of one particular dideoxynucleoside with its normal deoxynucleotide counterpart, and the three other deoxynucleoside triphosphates. The modified primer may or may not be immobilized to the solid support at this point. (Immobilization may occur either before or after the enzymatic extension reactions, depending on a number of experimental factors).

DEPR:

For reactions in which the modified primers were not immobilized to a solid support prior to enzymatic extension, immobilization is carried out as described in Section IIB above.

DEPR:

In an alternative embodiment, an array of the immobilized, cleavable primers can be formulated (Fodor, et al., 1991; Southern, et al., 1992). In this aspect of the invention, the array consists of the modified primers of the present invention where the cleavable linkage is, for example, a photocleavable linkage (e.g., backbone nitrobenzyl group) and the primer is attached to the support matrix through the immobilization site of the modified primer. In this embodiment, the target DNA molecule is hybridized to the primers, primer extension reactions carried out and the different sequence primers are sequentially cleaved and the presence or absence of an extension product is determined. When extension products are detected their sequences can be determined as described above.

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L3: Entry 7 of 12

File: USPT

Dec 15, 1998

DOCUMENT-IDENTIFIER: US 5849480 A

TITLE: Process and device for assaying a hapten

BSPR:

The term "solid support" as used here includes all polymeric materials onto which a nucleic acid fragment can be immobilized for use in diagnostic tests.

Natural or synthetic materials, chemically modified or otherwise, can be used as solid support, especially polysaccharides such as cellulose materials, for example paper, cellulose derivatives such as cellulose acetate and nitrocellulose; polymers such as poly(vinyl) chloride, polyethylene, polystyrenes, polyamides, polyacrylates, polyurethanes, polycarbonates, polytetrachloroethylenes, copolymers such as vinyl chloride-propylene, vinyl chloride-vinyl acetate polymers, copolymers based on styrene or substituted derivatives of styrene, and synthetic fibres such as nylon.

BSPR:

Using the direct manner, two approaches are possible, either by adsorption of the conjugate onto the solid support, that is to say by non-covalent bonds (mainly of the hydrogen, Van der Waals or ionic type), or by establishing covalent bonds between the conjugate and the support.

ORPL:

"Acridine-and Cholesterol-Derivatized Solid Supports for Improved Synthesis of 3'-Modified Oligonucleotides," Bioconjugate Chem., ol. 2 (1991) pp. 217-225.

WEST☐ Generate Collection

L3: Entry 6 of 12

File: USPT

Feb 16, 1999

DOCUMENT-IDENTIFIER: US 5871906 A

TITLE: Method for detection of amplified nucleic acid products and related diagnostic assays

DEPR:

The method for the detection of amplified nucleic acid products of the present invention includes the use of immobilized affinity molecules capable of binding (capture) hapten-labeled nucleotide or target molecule-labeled nucleotide that have been incorporated into amplified nucleic acid products during strand synthesis in an amplification process; and reaction of the unbound incorporated hapten-labeled nucleotide or target molecule-labeled nucleotide to affinity molecules conjugated to reporter compounds or enzymes which are visualized directly or by substrate color development. Steps in the process of the present invention include: immobilization of the affinity molecules to a solid support by covalent coupling or non-covalent adsorption; removal of unbound affinity molecules from the solid support using a wash step; blocking the surface areas of the solid support, not bound by affinity molecules, to prevent non-specific binding to the solid support surface by nucleic acids that may be present in the amplification reaction sample to be analyzed; addition and incubation of the sample to be analyzed with the modified solid support to allow reaction between the affinity molecules and hapten or target molecules contained in the added sample; a second wash step to remove nonspecifically bound hapten-labeled nucleotide or target molecule-labeled nucleotide, molecules not captured by the affinity molecules, as well as to remove other components, other than amplified nucleic acids, contained in the amplification reaction sample; addition and incubation of an affinity molecule conjugate to allow reaction with any unbound incorporated hapten or target molecules remaining from the preceding sequential steps; wherein said conjugate consists of either reporter molecules that can be directly visualized or enzyme that requires interaction with substrate for color development; a third wash step to remove unbound conjugate; and either direct visualization of the full process, or addition and incubation of substrate to allow reaction with any bound affinity conjugate present, resulting in color development to facilitate visualization of the full process.

CLPV:

(a) immobilizing affinity molecules to a solid support by covalent coupling or non-covalent adsorption;

CLPV:

(d) adding and incubating the sample to be analyzed with the modified solid support to allow reaction between the affinity molecules and hapten-labeled nucleotide or target molecule-labeled nucleotide contained in the sample;

WEST☐ Generate Collection

L3: Entry 3 of 12

File: USPT

Jun 12, 2001

DOCUMENT-IDENTIFIER: US 6245507 B1

TITLE: In-line complete hyperspectral fluorescent imaging of nucleic acid molecules

DEPR:

Holmstrom et al., for example, exploit the affinity of biotin for avidin and strepavidin, and immobilize biotinylated nucleic acid molecules to avidin/strepavidin coated supports (Holmstrom et al., Anal. Biochem. 209:278-283 (1993), herein incorporated by reference in its entirety). Another method requires the pre-coating of the polystyrene or glass solid phases with poly-L-Lys or poly L-Lys, Phe, followed by the covalent attachment of either amino- or sulfhydryl-modified oligonucleotides using bi-functional crosslinking reagents. Both methods require the use of modified oligonucleotides as well as a pretreatment of the solid phase (Running et al., Bio/Techniques 8:276-277(1990); Newton et al. Nucleic Acids Res. 21:1155-1162 (1993), both of which are herein incorporated by reference in their entirety).

DEPR:

Kawai et al. describe an alternative method in which short oligonucleotide probes were ligated together to form multimers and these were ligated into a phagemid vector (Kawai et al., Anal. Biochem. 209:63-69 (1993), herein incorporated by reference in its entirety). The oligonucleotides were immobilized onto polystyrene plates and fixed by UV irradiation at 254 nm. A method for the direct covalent attachment of short, 5' -phosphorylated primers to chemically modified polystyrene plates ("Covalink" plates, Nunc) has also been proposed by Rasmussen et al., Anal. Biochem. 198:138-142 (1991), herein incorporated by reference in its entirety. The covalent bond between the modified oligonucleotide and the solid phase surface is created by a condensation reaction with a water-soluble carbodiimide. The Rasmussen et al. method concerns a predominantly 5'-attachment of the oligonucleotides via their 5'-phosphates; however, it requires the use of specially prepared, expensive plates.

DEPR:

Under another preferred embodiment, the array can be created by means of a "gene pen". A "gene pen", as used herein, refers to a mechanical apparatus comprising a reservoir for a reagent solution connected to a printing tip. The printing tip further comprises a means for mechanically controlling the solution flow. Under one embodiment, a multiplicity of "gene pens" or printing tips may be tightly clustered together into an array, with each tip connected to a separate reagent reservoir. Under another embodiment, discrete "gene pens" may be contained in an indexing turntable and printed individually. Typically, the solid surface is pretreated to enable covalent or non-covalent attachment of the reagents to the solid surface. Preferably, the printing tip is a porous pad.

WEST☐ Generate Collection

L3: Entry 1 of 12

File: USPT

Nov 27, 2001

DOCUMENT-IDENTIFIER: US 6322968 B1

TITLE: De novo or "universal" sequencing array

DEPR:

Under one preferred embodiment, an attachment moiety (AM) is coupled to the 5' terminus of the sequencing reagent. The attachment moiety permits attachment of the sequencing reagent to the solid surface. However, the attachment moiety is not necessary to practice the present invention. Especially when the sequencing reagent is non-specifically attached to the solid surface. Under one of the preferred embodiments, the sequencing reagent is non-specifically attached to the solid surface. The sequencing reagent can be non-specifically attached to the solid surface by means of a cationic agent, such as octyl-dimethylamine HCL or NaCl. Alternatively, the sequencing reagent can be non-specifically attached to a charged surface, such as an amino modified solid surface.

DEPR:

Under one preferred embodiment, the sequencing reagent can be specifically attached to the solid surface by means of a non-covalent bond. For example, a biotin or iminobiotin labeled oligonucleotide may be immobilized to an avidin or streptavidin coated solid surface. Alternatively, a haptenated oligonucleotide may be immobilized to an antibody coated solid surface. However, it is to be understood that other ligand receptor interactions are suitable for use in the present invention.

DEPR:

Recently, several methods have been proposed as suitable for immobilizing an oligonucleotide to a solid support. Holmstrom, K. et al., for example, exploit the affinity of biotin for avidin and streptavidin, and immobilize biotinylated nucleic acid molecules to avidin/streptavidin coated supports (Holmstrom, K. et al., Anal. Biochem. 209:278-283 (1993), herein incorporated by reference). Another method requires the pre-coating of the polystyrene or glass solid phases with poly-L-Lys or poly L-Lys, Phe, followed by the covalent attachment of either amino- or sulfhydryl-modified oligonucleotides using bi-functional crosslinking reagents. Both methods require the use of modified oligonucleotides as well as a pretreatment of the solid phase (Running, J. A. et al., BioTechniques 8:276-277 (1990); Newton, C. R. et al. Nucleic Acids Res. 21:1155-1162 (1993), both of which are herein incorporated by reference).

DEPR:

Kawai, S. et al. describes an alternative method in which short oligonucleotide probes were ligated together to form multimers and these were ligated into a phagemid vector (Kawai, S. et al., Anal. Biochem. 209:63-69 (1993), herein incorporated by reference). The oligonucleotides were immobilized onto polystyrene plates and fixed by UV irradiation at 254 nm. A method for the direct covalent attachment of short, 5'-phosphorylated primers to chemically modified polystyrene plates ("Covalink" plates, Nunc) has also been proposed by Rasmussen, S. R. et al. (Anal. Biochem. 198:138-142 (1991), herein incorporated by reference). The covalent bond between the modified oligonucleotide and the solid phase surface is created by a condensation reaction with a water-soluble carbodiimide. The Rasmussen method claims a predominantly 5'-attachment of the oligonucleotides via their 5'-phosphates; however, it requires the use of specially prepared, expensive plates.

DEPR:

Under another preferred embodiment, the array can be created by means of a "gene pen". A "gene pen", as used herein, refers to a mechanical apparatus comprising a reservoir for a reagent solution connected to a printing tip. The printing tip further comprises a means for mechanically controlling the solution flow. Under one embodiment, a multiplicity of "gene pens" or printing tips may be tightly clustered together into an array, with each tip connected to a separate reagent reservoir. Under another embodiment, discrete "gene pens" may be contained in an indexing turntable and printed individually. Typically, the solid surface is pretreated to enable covalent or non-covalent attachment of the reagents to the solid surface. Preferably, the printing tip is a porous pad.

DEPR:

By using an array of nested sequencing primers, it is possible to modify the GBA method for use in the present invention to sequence large segments of a template nucleic acid molecule simultaneously. By aligning the extension products of the nested primers, one of skill in the art can determine the sequence of the unknown target sequence. The general strategy of sequencing by aligning nested primers is disclosed by Sapolsky, R. J. et al., Genomics 33:445-456 (1993), Pease, A. C. et al., Proc. natl. Acad. Sci. (U.S.A.) 91:5022-5026 (1994) and Bains, W., GATA 10:84-93 (1993), all of which are herein incorporated by reference.

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nested terms that are not separated by a logical operator.

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L5 1 L2 AND (NON (10A) COVALEN##)

=> s l5 and (bind? or attach? or adsor?)
L6 1 L5 AND (BIND? OR ATTACH? OR ADSOR?)

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L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
AN 1991:488658 CAPLUS
DN 115:88658
TI The influence of poly(ethylene oxide) spacers on the **covalent**
and **non-specific binding** of immunoglobulin G to silica
surfaces
AU Kopeckova, P.; Kopecek, J.; Andrade, J. D.
CS Dep. Bioeng., Univ. Utah, Salt Lake City, UT, 84112, USA
SO New Polym. Mater. (1990), 1(4), 289-97
CODEN: NPMAE8
DT Journal
LA English
AB Porous silica beads coated with 3-aminopropyltriethoxysilane (APS) were
modified with excess glutaraldehyde followed by reaction with an excess of
1 of the following compds: 1,2-diaminoethane; .alpha.,.omega.-
diaminopoly(ethylene oxide), Mr = 1000; and .alpha.,.omega.-

diaminopoly(ethylene oxide), $M_r = 5000$. By this procedure, beads were prepd. that contained spacers terminated in primary amino groups. The influence of the spacer structure on the nonspecific sorption of ^{125}I -labeled human IgG was studied. Whereas the amt. of IgG bound to beads modified with 1,2-diaminoethane was comparable to the **adsorption** on APS modified beads, the nonspecific **adsorption** decreased when PEO spacers were introduced. PEO5000 was more effective in decreasing the nonspecific sorption of IgG than PEO1000. The **beads** contg. spacers terminated in **amino** groups were **modified** with glutaraldehyde again and ^{125}I -labeled IgG was bound covalently. The amt. of IgG bound was independent of the structure of the spacer. Desorption studies indicated that under the conditions used for covalent **binding** the nonspecific **binding** was minimal. The time dependence of both types of **binding** on beads contg. the PEO5000 spacer was detd.

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